approved by the institutional review board, and written informed consent was obtained from each subject before the study.
Results: Plasma concentration of MNA, renal creatinine clearance, and CLTS,MNA were 9.9 (8.1) ng/mL, 139 mL/min/1.66 m^2, and 181 (110) mL/min/1.66 m^2, respectively, indicating that the tubular secretion of MNA is involved in its renal clearance. Eight SNPs, –151C>A, –66T>C, 191G>A, 373C>T, 708C>T, 1490G>C, IVS5–12G>C, and IVS5–4G>A, were detected on *SLC47A1* gene with minor allele frequencies of 0.009, 0.194, 0.009, 0.009, 0.083, 0.009, 0.343, and 0.463, respectively. A loss-of-function allele of *SLC22A2*, 808G>T, was detected with minor allele frequency of 0.105 and 1 subject was found having this variant as homozygote. She showed almost null $CL_{TS,MNA}$; therefore, this subject was excluded from the analysis. Seventeen subjects having either –66C/C or T/C alleles showed a trend toward reduced $CL_{TS,MNA}$ compared with those having the wild-type genotype (151 [IQR, 107–167] vs 184 [115–227] mL/min/1.66 m^2; $P = 0.08$). Other variants showed no appreciable effects on $CL_{TS,MNA}$.
Conclusion: We consider that $CL_{TS,MNA}$ may be a useful biomarker of the activity of renal organic cation transporters. The –66C allele of hMATE1/*SLC47A1* may contribute to reduced renal clearance of MNA in healthy subjects not having homozygous 808G>T variant of hOCT2/*SLC22A2*.
Disclosure of Interest: None declared.

PP138—ANALYSIS OF CYP2D6 GENETIC POLYMORPHISMS IN MEXICAN MESTIZOS, LACANDONES AND TZELTALES

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Introduction: More than 80 allelic variants have been described for *CYP2D6* that result in poor (PM), efficient or extensive (EM) and ultrarapid (UM) metabolizers of CYP2D6 drug substrates. The distribution of PMs, Ems, and UMs varies markedly among human populations; however, it has been particularly difficult to determine in countries with wide ethnic diversity. Currently, the Mexican population is composed of Mestizos (≈90%) and >85 different ethno linguistic indigenous populations (Mexican-Amerindians). Lacandones and Tzeltales are Mexican indigenous individuals that inhabit the state of Chiapas.
Aim: To perform a genetic analysis of *CYP2D6* to determine the frequency of the hypothetical PM and UM status in Lacandones, Tzeltales, and 2 mestizo populations and compare it with previously reported Mexican populations.
Patients (or Materials) and Methods: The *CYP2D6* genotype was analyzed in 154 Mexican Lacandones (ML), 26 Tzeltales (MT), 249 Mexican Mestizos from Central Mexico (MM1), and 100 Mexican Mestizos from Chiapas (MM2) healthy volunteers. All participants gave informed consent before its participation. The study was approved by the local ethical committee. Genomic DNA was extracted from blood samples by standard techniques. *CYP2D6* genotyping was performed by PCR for *CYP2D6*5* and multiplication alleles, TaqMan® assays (AB) were used for *CYP2D6*2, *3, *4, *6, *10, *17, *35, *41* and copy number variations. Differences in *CYP2D6* allele frequencies were compared by using the chi-square ($\chi 2$) test and/or Fisher's exact test. Statistical analysis was done by STATISTICA 4.3 and GraphPad Prism 3.02 softwares.
Results: The PM frequency was very low in MM1 (0.8%) and MM2 (1%), while it was absent from MLs and MTs in a manner similar to 0% previously found in Tepehuanos and in other Mexican Amerindian populations. The UM phenotype frequency in MLs was also very similar to Tepehuanos (1.3% and 1.5%, respectively) and to Mexican American populations previously studied. In MTs the UM frequency was 0%, while MM1 and MM2 showed a 5.6% and 3.0 frequency, respectively.
Conclusion: These data indicate that the frequencies of *CYP2D6* PM and UM predicted phenotypes are very similar between Tepehuanos, Lacandones, and Tzeltales, but differ from Mexican Mestizos from Central and Southeastern Mexico. The predicted PM phenotype was very similar between MM from Central and Southeastern Mexico but varied in the frequency of UM. These findings reveal Mexican populations diversity that could have important implications in drug response to CYP2D6 substrates.
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PP139—ASSOCIATION OF ABCB1, ABCC2, CYP2C9 AND CYP2C19 POLYMORPHISM WITH PHENYTOIN PLASMA CONCENTRATIONS

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Introduction: Epilepsy is the most prevalent chronic neurologic disorder that affects 65 million people worldwide. Phenytoin (PHT) is 1 of the most widely prescribed antiepileptic drugs (AEDs); however, large interindividual variability in doses and concentrations has been observed in epilepsy treatment with PHT. Functional polymorphisms in genes encoding drug-metabolizing enzymes, drug transporters, and drug targets have been suggested to contribute to this genetic variability.
Aim: To evaluate the association of *CYP2C9*, *CYP2C19*, *ABCB1*, and *ABCC2* polymorphism on PHT plasma levels in epileptic patients.
Patients (or Materials) and Methods: The present investigation was carried out in 57 consecutive patients (16–65 years) suffering epilepsy and treated with phenytoin. Approval from the institutional biomedical research ethics committee and the informed consent of patients was obtained before enrollment into the study. Genomic DNA was isolated from blood samples by standard technique. Genotyping of *CYP2C9*2, CYP2C19*2* and **3, ABCB1 C1234T, C3435T, G2677A/T, ABCC2 G24A*, and *G1249A* was performed by real-time

PCR using allele-specific probes, and *CYP2C9*3* by PCR-RFLP. PHT plasma levels were determined by radioimmunoassay.
Results: Twenty-six patients showed PHT therapeutic levels (10–20 µg/mL), 24 subtherapeutic and 7 supratherapeutic. Three cases, 2 *CYP2C9 *1/*2*, and 1 *CYP2C19*1/3*, had subtherapeutic levels. Patients with wild-type *ABCB1* and ABCC2 genotypes exhibited a tendency to have increased PHT plasma levels than patients with mutant genotypes.
Conclusion: PHT plasma levels showed great variability among patients that was not statistically significant correlated to the genetic polymorphisms analyzed, although *ABCB1* and *ABCC2* wild-type genotypes showed a trend toward higher levels. Further investigations are needed with other candidate genes and a larger sample.
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Disclosure of Interest: None declared.

PP140—THE CONTRIBUTION OF PLATELET GLYCOPROTEINS (GPIA C807T AND GPIBA C-5T) AND CYCLOOXYGENASE 2 (COX-2 G--765C) POLYMORPHISMS TO PLATELET RESPONSE IN PATIENTS TREATED WITH ASPIRIN

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Introduction: Aspirin is an antiplatelet agent commonly used in treatment of patients with high risk to develop stroke and myocardial infarction. However, interindividual variability regarding the inhibition of platelet function by aspirin is well documented. In this study, the correlation between platelet glycoproteins (*GPIa* C807T and *GPIba* C-5T) and cyclooxygenase 2 (*COX-2* G-765C) polymorphisms and antiplatelet response in patients treated with aspirin was investigated.
Patients (or Materials) and Methods: Jordanian adult patients (n = 584) who are taking aspirin as an antiplatelet agent participated in the study. Platelet aggregation response was measured using Multiplate Analyzer® system. Polymerase chain reaction–restriction fragment length polymorphism assay (PCR-RFLP) was used for genotyping of the examined polymorphisms.
Results: Aspirin resistance was found in 15.8% of patients. Response to aspirin was significantly associated with *GPIba* C-5T polymorphism ($P < 0.05$). However, the *GPIa* C807T and *COX-2* G-765C polymorphisms were not related to aspirin resistance ($P > 0.05$).
Conclusion: A considerable fraction of the Jordanian population is resistant to the antiplatelet effect of aspirin, which might be related to *GPIba* C-5T polymorphism.
Disclosure of Interest: None declared.

PP141—THE RELEVANCE OF PLATELET GLYCOPROTEIN GP IIB/IIIA POLYMORPHISM TO ANTI-PLATELETS RESPONSE IN ACUTE CORONARY SYNDROME[ACS]

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Introduction: Pharmacogenomics is intervening in cardiovascular therapeutic armamentarium to tailor therapy to individual's genetic makeup. Accordingly, the potential implication of PlA gene variants of GPIIIa of platelet GP IIb/IIIa as a genetic risk factor provocateur and/or a therapeutic outcome modulator to antiplatelet therapy in ACS was probed.
Patients (or Materials) and Methods: Study enrolled 22 controls and 44 ACS patients (NSTEMI vs STEMI). They were risk stratified (TIMI score), sampled for genotyping and estimation of platelet aggregation and oxidative indices, then subdivided according to add-on antiplatelet therapy into: clopidogrel or tirofiban subgroups. After 48 hours, the therapeutic outcome was assessed; clinically [pain relief or complication prevalence (symptomatic, electrocardiographic, or hemorrhagic) and the investigational estimates were re-assessed. Intraprocedural evaluation of chest pain, ECG tracing, and angiographic findings (thrombus extent, TIMI flow, myocardial blush) were reported in patients who underwent percutaneous intervention [PCI].
Results: Frequency of PlA2 vs PlA1 allele was higher in ACS patients (significant in <60 years /doubled in STEMI vs NSTEMI). TIMI score, stratification permitted considering PlA2 variant as independent risk factor in UA/NSTEMI subsets. This was fostered by intraprocedural finding of more stenotic and thrombotic lesions in PlA2 carriers. A lack of significant association between PlA variants and changes in platelet aggregation or oxidative indices, debate their causal relation to PlA2 variant being an ACS risk factor. A positive correlation was observed between PlA variants and the therapeutic response outcome to both clopidogrel and tirofiban regarding platelet aggregation and relief of chest pain while their antioxidative potentiality was negatively correlated only to PlA1 carriers.
Conclusion: PlA2 variant could be considered a genetic risk factor contributor rather than an antiplatelet therapeutic response modulator when speaking of ACS. This awaits larger scale pharmacogenomic studies before a final statement is declared so as to individualize antiplatelet therapy to the best of its therapeutic outcome in ACS settings.
Disclosure of Interest: None declared.

PP142—INFLUENCE OF THE CYP2D6 -1584C>G PROMOTER POLYMORPHISM ON THE PHENOTYPE OF DEBRISOQUINE IN HEALTHY VOLUNTEERS FROM CUBA AND NICARAGUA

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Introduction: Ultrarapid drug metabolism (UM) mediated by CYP2D6 is associated with duplicated or amplified functional *CYP2D6* alleles. However, duplicated *CYP2D6* alleles only explains a fraction (10%–30%) of the UM phenotype observed in Caucasian populations, and other biochemical and/or genetic factors involved in UM phenotype remain unexplained yet. *CYP2D6 -1584C>G* has been related with changes in *CYP2D6* expression, being *-1584G* associated with higher expression. The aim of this study was to explore the relationship between *CYP2D6 -1584C>G* polymorphism and the debrisoquine hydroxylation capacity.